

***Remarks***

Reconsideration of this Application is respectfully requested. The Amendment places the application in condition for allowance or removes issues for appeal. Entry is respectfully requested.

Upon entry of the foregoing amendment, claims 26, 33, 117, 122-125, 137-147 and 149-161 are pending in the application, with claim 26 being the independent claim. Claims 28, 118-121, 127-136, and 148 are being cancelled herein without prejudice to or disclaimer of the subject matter therein. Claims 152-161 are being added, and claims 26, 33, 117, and 122-125 are being amended. It is believed these changes introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and request that they be withdrawn.

***Objections to the specification - sequence listing***

The Office Action, at page 2, maintained that the present application is not in compliance with the sequence rules. The concern expressed in the Office Action is that the "specification discusses several specific mutants of some reverse transcriptase at specific amino acid residues without identifying the amino acid sequence from which those residues are from" and that "[w]ithout identifying a specific amino acid sequence, at least to reference the numbering system for the amino acid, one of ordinary skill in the art would not be able to understand the specification." (Paper 49, p. 2.) Applicants respectfully disagree with the objection.

Applicants again point out that the mutated residues recited in the specification correspond to *known, conserved* positions in RSV reverse transcriptase. These known, conserved positions were described in Johnson *et al.*, as discussed in the Amendment and Reply filed July 21, 2003.

Regarding the GenBank accession numbers, even assuming that revisions of the database are an issue, the artisan can consult the publications cited in the database entries to obtain the original sequences (see attachments to Amendment and Reply filed July 21, 2003). Therefore, one of ordinary skill could not possibly misunderstand the specification.

Moreover, the MPEP expressly states:

In those instances in which prior art sequences are only referred to by name and a publication or accession reference, they need not be included as part of the "Sequence Listing," unless an examiner considers the referred-to sequence to be "essential material," per MPEP § 608.01(p). MPEP § 2422.03 at 2400-34, col. 2 (Aug. 2001). In this case, the Examiner has not stated that the referred-to sequences are essential. Therefore, according to the sequence listing rules, Applicants need not include the sequences in the sequence listing.

Accordingly, reconsideration and withdrawal of the objection are respectfully requested.

***Rejections under 35 U.S.C. § 112, first paragraph - written description***

Claims 26, 28, 33, 117-125, and 127-151 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the

specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. (Paper 49, p. 3.) Applicants respectfully traverse the rejection.

The Office Action addressed several points, which will be discussed below in turn.

The Office Action stated that the Declaration Concerning the Deposited Biological Material was not included with the Amendment and Reply filed on July 21, 2003. (Paper 49, p. 3.) Applicants enclose a courtesy copy of the Declaration (a copy of the date-stamped postcard is also enclosed, evidencing the filing of the Declaration on July 21, 2003). Therefore, this basis for rejection has been obviated.

The Office Action also stated that Johnson *et al.* does not teach the RNase H domain of AMV reverse transcriptase. (Paper 49, p. 3.) Applicants respectfully disagree.<sup>1</sup> Applicants point out that claim 26 was previously amended to omit the phrase "having RNase H activity" and the claims reciting "having reduced or substantially reduced RNase H activity" have been cancelled. None of the pending claims recite these phrases. Thus, this basis for rejection has been rendered moot.

Additionally, the Office Action stated that the prior art is irrelevant in a written description context. (Paper 49, p. 3.) Applicants respectfully disagree and refer the Examiner to opinions by the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") such as *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313 (Fed. Cir. 2003). In *Amgen*, the Federal Circuit instructed that functional descriptions of biological material can satisfy the written description requirement if a structure/function correlation

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<sup>1</sup> Applicants also reserve the right to establish that this publication does describe the AMV reverse transcriptase RNase H domain.

is *known in the art*. 314 F.3d at 1332. ("Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the *knowledge of the art* the disclosed function is sufficiently correlated to a particular, known structure." (emphasis added) (citation omitted)). Thus, contrary to the Examiner's statement, the prior art is relevant in the context of a written description rejection.

Concerning monomeric and multimeric forms of AMV reverse transcriptase, Applicants have cancelled claims 28, 118-121, and 148. The pending claims do not require a monomeric or multimeric AMV reverse transcriptase to be formed. Therefore, this basis for rejection has been rendered moot.<sup>2</sup>

The Office Action stated that the specification does not describe the  $\beta p4$  subunit by structural or chemical features. (Paper 49, p. 4.) Applicants have cancelled the claims that recited this term (claims 28, 120 and 148). Therefore, this basis for rejection has been rendered moot.

Applicants assert that the specification adequately describes the claimed invention. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

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<sup>2</sup> Concerning Grandgenett *et al.* and Soltis *et al.*, Applicants respectfully disagree with the Examiner's interpretation and reserve the right to establish that these publications do teach a monomeric form of reverse transcriptase. Additionally, Applicants assert that Lin *et al.*, *J. Biol Chem.* 266:1635-1640 (1991) teach active AMV reverse transcriptase in the multimeric  $(\alpha\beta)_2$  form in the abstract on page 1653, column 1, paragraph 2, page 1639 (An active  $(\alpha\beta)_2$  form was detected in sedimentation velocity experiments).

***Rejections under 35 U.S.C. § 112, second paragraph***

Claims 28, 33, 117-121, 124, 125, and 127-151 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting the phrase "one or more subunits" and " $\beta$ p4 subunit." (Paper 49, pp. 4-5.) Applicants respectfully traverse the rejection.

Contrary to the Examiner's assertion, none of the rejected claims recites "one or more subunits."<sup>3</sup> Additionally, as noted above, AMV reverse transcriptase in the  $(\alpha\beta)_2$  form is enzymatically active, contrary to the assertion on page 4 of the Office Action that "there could not be more than two subunits per molecule of enzyme." Therefore, this portion of the rejection is in error.

Concerning " $\beta$ p4 subunit," the claims reciting this term (claims 28, 120, and 148) have been cancelled. Therefore, this basis for rejection has been rendered moot.

Applicants assert that the claims are clear and definite. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

***Rejections under 35 U.S.C. § 103***

Claims 26, 28, 33, 117-119, 121-125, and 127-151 were rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Soltis *et al.* in view of the state of the art. (Paper 49, p. 6.) Applicants respectfully traverse the rejection.

Soltis *et al.* disclose the expression in *E. coli* of the AMV reverse transcriptase  $\alpha$  subunit, the expression in *E. coli* of the AMV reverse transcriptase  $\beta$  subunit, and the

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<sup>3</sup> Although claim 28 (now cancelled) recited "at least one subunit," the language did not require the reverse transcriptase produced in the claimed method to be a monomer or a multimer, contrary to the Examiner's assertion. The phrase only modified the nucleic acids recited in claim 26, from which claim 28 depended.

purification of each to a specific activity 10,000-100,000 fold lower than the specific activity of AMV reverse transcriptase purified directly from AMV particles. Soltis *et al.* also disclose the expression and purification of the full length *pol* product in *E. coli*.

The pending claims are directed to a method of producing AMV reverse transcriptase by expressing the  $\alpha$  and  $\beta$  subunits, *together*, in a eukaryotic cell, and isolating or purifying the expressed reverse transcriptase, such that the resulting AMV reverse transcriptase has a specific activity of at least about 30,000 units per milligram. Thus, the present claims recite (1) expressing the  $\alpha$  subunit, and (2) expressing the  $\beta$  subunit, (3) in the same eukaryotic cell, and (4) isolating or purifying AMV reverse transcriptase having a specific activity of  $\geq 30,000$  units per milligram. Soltis *et al.* do not teach or suggest all four limitations. Further, there was no motivation to modify Soltis *et al.* based on the knowledge in the art.

Applicants therefore respectfully assert that the present method is non-obvious over the prior art. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

#### ***Other Matters***

Concerning the statement, "it appears that the applicants could not produce and purify the AMV-RT from transformed insect cells with a specific activity of greater than 57,500 units/mg of protein, presumably, their best effort," on page 7 of the Office Action, Applicants respectfully traverse. There is no basis for the presumption that the published results represent Applicants' best effort, or that Applicants are unable to obtain

specific activity greater than 57,500 units/mg. Applicants request that the Examiner either withdraw the statement or provide evidence to support it.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and request that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Helene C. Carlson  
Agent for Applicants  
Registration No. 47,473

Date: 5/3/04

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Gerard *et al.*

Appl. No. 09/245,026

Filed: February 5, 1999

For: **Compositions and Methods for  
Reverse Transcription of Nucleic  
Acid Molecules**

Art Unit: 1637

Examiner: Strzelecka, T.

Atty. Docket: 0942.4330004/RWE/MTT

**Declaration Concerning the Deposited Biological Material**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

I, Alan W. Hammond, on behalf of Invitrogen Corporation, having business concerns at 1600 Faraday Avenue, Carlsbad, California 92008, declare and state as follows:

*Escherichia coli* DH10B(pDABH-His) was deposited under the terms of the Budapest Treaty on April 15, 1997. This deposit was made at the Agricultural Research Culture Collection (NRRL) International Depositary Authority, 1815 N. University Street, Peoria, Illinois 61604, and given accession number NRRL B-21679. *Escherichia coli* (pDAMVABH-) was deposited under the terms of the Budapest Treaty on June 17, 1997. This deposit was made at the Agricultural Research Culture Collection (NRRL) International Depositary Authority, 1815 N. University Street, Peoria, Illinois 61604, and given accession number NRRL B-21790.

Assurance is hereby given that: (1) all restrictions on the availability to the public of the deposited materials will be irrevocably removed upon the granting of a patent, subject to 37 C.F.R § 1.808(b); (2) the materials have been deposited under conditions such that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto; and (3) the deposits will be maintained with all of the care

necessary to keep them viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposit, and in any case, for a period of at least thirty years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

I have read and understood 37 C.F.R. § 10.18(b) and (c).

Respectfully submitted,

Date: October 2, 2002

By: Alan W. Hammond

Alan W. Hammond, Esquire  
Chief Intellectual Property Counsel  
Invitrogen Corporation

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BUDAPEST TREATY ON THE INTERNATIONAL  
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS  
FOR THE PURPOSE OF PATENT PROCEDURES

INTERNATIONAL FORM

**TO**  
 Dr. Alan Hammond  
 Life Technologies, Inc.  
 9800 Medical Center Drive  
 Rockville, MD 20850

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT  
 issued pursuant to Rule 7.1 by the  
 INTERNATIONAL DEPOSITORY AUTHORITY  
 identified at the bottom of this page

**NAME AND ADDRESS  
OF DEPOSITOR**

**I. IDENTIFICATION OF THE MICROORGANISM**

Identification reference given by the  
DEPOSITOR:

Accession number given by the  
INTERNATIONAL DEPOSITORY AUTHORITY:

*Escherichia coli DH10B(pDABH-His)*

NRRL B-21679

**II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION**

The microorganism identified under I. above was accompanied by:

a scientific description

a proposed taxonomic designation

(Mark with a cross where applicable)

**III. RECEIPT AND ACCEPTANCE**

This International Depository Authority accepts the microorganism identified under I. above, which was received by it on April 15, 1997(date of the original deposit)<sup>1</sup>

**IV. RECEIPT OF REQUEST FOR CONVERSION**

The microorganism identified under I. above was received by this International Depository Authority on (date of the original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).

**V. INTERNATIONAL DEPOSITORY AUTHORITY**

Name: Agricultural Research Culture  
Collection (NRRL)  
International Depository Authority

Address: 1815 N. University Street  
Peoria, Illinois 61604 U.S.A.

Signature(s) of person(s) having the power  
to represent the International Depository  
Authority or of authorized official(s):  
*J. L. Sager*

Date:

11-14-97

<sup>1</sup> Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired.

6947-493256

BUDAPEST TREATY ON THE INTERNATIONAL  
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS  
FOR THE PURPOSE OF PATENT PROCEDURES

INTERNATIONAL FORM

TO  
Life Technologies, Inc.  
Attn: Dr. Alan Hammond  
P. O. Box 6482  
9800 Medical Center Drive  
Rockville, MD 20850

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT  
issued pursuant to Rule 7.1 by the  
INTERNATIONAL DEPOSITORY AUTHORITY  
identified at the bottom of this page

NAME AND ADDRESS  
OF DEPOSITOR

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR:	Accession number given by the INTERNATIONAL DEPOSITORY AUTHORITY:
<i>Escherichia coli</i> (pDAMVABH)	NRRL B-21790

II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

- a scientific description  
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Address: 1815 N. University Street  
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Signature(s) of person(s) having the power  
to represent the International Depository  
Authority or of authorized official(s):

Date:

*J. L. Dugay*  
7-6-97

<sup>1</sup> Where Rule 6.4(d) applies, such date is the date on which the status of international depository authority was acquired.



Applicants: Gerard *et al.*

Application No.: 09/064,057

Filed: April 22, 1998

For: Recombinant Methods for Making Reverse Transcriptases and Mutants Thereof

Due Date: July 21, 2003

Art Unit: 1652

Examiner: Nashed, N.T.

Docket: 0942.4330002

Atty: RWE/HCC

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter;
2. Fee Transmittal Form (PTO/SB/17);
3. Petition For Extension of Time Under 37 C.F.R. § 1.136(a)(1);
4. Request For Continued Examination (RCE) Transmittal;
5. Amendment and Reply Under 37 C.F.R. § 1.116 in the Revised Format of the Pre-OG Notice Dated January 31, 2003 with attached Exhibits;
5. A copy of the Declaration Concerning the Deposited Biological Material;
6. An executed Certificate Under C.F.R. § 3.73(b);
7. PTO Credit Card Form in the amount of \$860.00 for: \$110.00 for the one month Extension of Time fee; and \$750.00 for the Request For Continued Examination (RCE); and
8. One return postcard.



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